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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/752,292	12/28/2000	Alex Chenchik	CLON-017US2	6642

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Bret Field
BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025

EXAMINER
ZITOMER, STEPHANIE W

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/752,292	CHENCHIK et al.
Examiner	**Art Unit**
S. Zitomer	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 29, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-27* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Priority

1. Applicant's claim for priority based on provisional application serial no. 60/181,366 is acknowledged. It is noted that claims 1-9 and 12-27 are not entitled to the earlier filing date of the provisional application because the latter does not provide written description of a representative number of species of the large "analyte" genus.

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-15 lack antecedent basis in step (a) for steps (b) and (c) because in step (a) a pre-formed analyte:ligand:tag complex is bound to a solid support via hybridization of the tag to the tag complement on the support and thus there is no antecedent for "analyte in said sample" in step (c) nor is there a rationale for "detecting" in step (b). The preamble does not remedy the deficiency because it simply recites a use for the method. It is suggested to combine claims 1 and 2.

(b) Claims 1-15 are further confusing because step (a) recites "producing" a hybridization complex on the surface of an array whereas the claim does not recite method steps for "producing" the complex. See below at (d).

(c) Claims 1-15 are confusing in appearing to be missing the word "of" at step (b).

(d) Claim 2 is confusing in lacking positive method steps. It is unclear whether some entity is "produced" or whether a nondescript sample is simply "contacted" with some particular reagents. Method claims need not recite all operating details but should at least recite **positive, active** steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter

the claims encompass as well as make clear the subject matter from which others would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at 6.

(e) Claim 3 is confusing in that it does not appear to be further limiting of claim 1. Claim 1 recites that the tag and tag complement **hybridize** and therefore are taken to be nucleic acids. If applicant is aware of other types of molecules that **hybridize** such information should be provided as it may raise a written description issue. If not, claim 3 should be canceled.

(f) Claim 11 is confusing in that it does not appear to be further limiting of claim 10. Claim 10 recites "said analyte is a polypeptide". As a polypeptide is a protein by definition it is unclear how reciting that the "polypeptide is a protein" further limits the polypeptide. If applicant is aware of other types of polypeptides that are not proteins such information should be provided as it may raise a written description issue. If not, claim 11 should be canceled.

(g) Claim 12 lacks antecedent in claim for "tagged affinity ligands comprise an antibody or binding fragment thereof" because claim 1 does not recite an analyte to which the antibody or binding fragment correspond, i.e., an analyte that would be expected to bind to the recited affinity ligand. It is suggested to include a corresponding analyte in claim 1.

(h) Claim 14 recites a further use of the method recited in the preamble of claim 1 which is not a patentable limitation. It is suggested to recite the "plurality" in the method steps.

(I) Claims 16-21 lack antecedent basis in (a) for (b) because the latter recites means involving **both** the array and the set of tagged affinity ligands whereas (a) recites only one of them. It is suggested to recite that both (I) and (ii) are present in (a) by combining claims 16 and 17.

(j) Claim 23 is confusing in that it does not appear to be further limiting of claim 22. Claim 22 recites that the tag and tag complement **hybridize** and therefore are taken to be nucleic acids. See above at (e).

(k) Claims 25-27 fail to define the claimed invention with particularity in that "gene affinity ligand" is not defined in the claims or in the specification. Thus one of skill in the art would not be apprised of the scope of the claimed invention.

Rejection under 35 U.S.C. 102(e): Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

3. Claims 1-3, 10, 11 and 13-17 are rejected under 35 U.S.C. 102(e) as being anticipated by the patent to Burmer (6,087,103). Regarding claims 1-3, Burma discloses the method of detecting at least one analyte in a sample comprising (a) forming a population of complexed analyte/tagged affinity ligand wherein the tag is an oligonucleotide (nucleic acid); (b) capturing the complexes on a solid support by hybridizing the tags with tag complements attached to the solid support; (c) detecting the at least one analyte by relating the complexes captured on the support to determine the presence of the at least one analyte (columns 16-17, claim 13. Regarding claims 10 and 11, the patent discloses that the analyte is a polypeptide (protein) (columns 17-18, claim 17). Regarding claim 13, the patent discloses that the tag is labeled (column 17, claim 15). Regarding claim 14, the patent discloses the method as a method of determining the presence of a plurality of analytes (column 1, lines 47-50). Regarding claim 15, the patent discloses that the plural analytes are proteins (column 1, lines 57-60). Regarding claims 16 and 17, the patent discloses the claimed kits comprising at least one of an array of distinct tag complements immobilized on the surface of a support and a set of distinct tagged affinity ligands plus a means for identifying the physical location on the array to which each distinct tagged affinity ligand hybridizes (column 15, lines 8-15, column 11, lines 15-23).

Rejections under 35 U.S.C. 103(a): Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 4-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burmer as applied to claims 1-3, 10, 11 and 13-17 above, and further in view of Shannon et al. (6251,588) and Lockhart et al. (6,333,155). The claim 1 method embodiments of claims 4-9 differ from that of Burmer wherein any difference in hybridization efficiency between any two tag/tag complements does not exceed about 10 fold (claim 4), about 5 fold (claim 5) or about 3 fold (claim 6) and wherein the level of cross-hybridization of any tag employed in the method does not exceed about 10% (claim 7), about 2% (claim 8) or about 1% (claim 9). However, the practice of optimizing hybridization efficiency and minimizing cross-hybridization in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefit of maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court

found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results. Regarding claim 12, the claimed invention method differs from that of Burmer wherein the tagged affinity ligands comprise an antibody or binding fragment thereof. However, in view of routine practice in the art of ligand binding assays in which the ligand for an analyte protein is an antibody the skilled practitioner would have been motivated to employ an antibody as the ligand for the protein analyte in the Burmer method. One of ordinary skill in the art would have been motivated further by the ready availability for example in commercial sources of antibodies to many proteins as well as by the routinely practiced methods of producing antibodies.

5. Claims 18-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burmer as applied to claims 1-17 above (paragraphs 3 and 4) and further in view of Shannon et al. (6251,588), Lockhart et al. (6,333,155) and further in view of Brown et al. (Nat. Gen. Suppl. 21:33-37, Jan. 1999). Regarding claims 18, 19 and 22-26 the claimed invention kit, tag complement array and tag set differ from those of Burmer wherein the magnitude of difference in hybridization efficiency between any two tag/tag complement pairs does not exceed about 10 fold and any tag in the set of tagged affinity ligands has a level of cross-hybridization with respect to the array that does not exceed 10%. However, the practice of optimizing hybridization efficiency and minimizing cross-hybridization in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefit of

maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results. Regarding claim 20 and 21, the claimed invention kit differs from that of Burmer wherein the means for identifying the physical location on the array comprises a medium that includes identifying information or a means for remotely assessing the information is provided in the kit wherein the latter is a website address. However, it would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to include printed information such as a website address in the kit in view of routine practice in the art of accessing public nucleotide sequence databases for sequence searching for the obvious benefit of obtaining a large amount of sequence information in a readily available format. For example, Brown et al. teach that the use of molecular arrays generates a large amount of information which may be managed and published via websites. Regarding claim 24, the claimed invention array differs from that of Burmer wherein the array has a density that does not exceed about 400 spots/square cm. However, oligonucleotide arrays routinely used in the prior art were known to have densities ranging from less than 100 to more than 1000 spots per square cm. Therefore, one of ordinary skill in the art at the time the claimed invention was made would have been motivated according to personal preference to select an array density appropriate to particular experimental parameters for the obvious benefit of optimizing results. Regarding claim 27, the claimed invention set of tagged affinity ligands comprises at least 20 distinct tagged ligands. Burmer teaches this embodiment in Figure 1.

Prior art of interest

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The patent to Kamb et al. (6,060,240) is cited for the use of capture tags which have complementary tags attached to solid support wherein the tag sequences are selected to have minimal cross-hybridization (column 6, line 47-column 7, line 4; columns 40-41, claim 1).

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 8:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stephanie Zitomer, Ph.D.
January 28, 2002